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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/597,357	07/21/2006	Hiroaki Shimokawa	P30188	9832

7055 7590 02/05/2009

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EXAMINER	
FINN, MEGHAN R	
ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
02/05/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/597,357	SHIMOKAWA, HIROAKI	
	Examiner	Art Unit	
	MEGHAN FINN	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *November 21, 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) *1-4* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 July 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/30/06; 7/28/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse of Group II (claims 5-8) in the reply filed on November 21, 2008 is acknowledged.

Claims 1-4 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on November 21, 2008.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of vasospasms, does not reasonably provide enablement for *prevention* of vasospasms. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Applicant has claimed a method of prevention or treatment for vasospasm accompanying a bypass operation. While applicant is enabled for treatment of vasospasm accompanying a bypass operation, they have not shown how one of skill in

the art would be able to use fasudil or hydroxyfasudil to prevent such vasospasm. Prevention reads upon stopping the spasms from ever occurring which applicant has not even attempted to address, only administering fasudil after the start of the vasospasms. Furthermore, simply because the patient who was administered fasudil did not develop more vasospasm in the days after surgery which were monitored does not mean that they were prevented. One of skill in the art would expect that after the vasospasms which were caused by the surgery were treated as demonstrated that there would be no reason for more to occur. Applicant has not shown that their examples prevented such spasms from reoccurring but more importantly they have not provided any direction which would enable one of skill in the art to prevent such vasospasms from occurring.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in *In re Wands*, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount of direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The quantity of experimentation necessary to develop a method of prevention would be large (1) due to the lack of direction or examples towards prevention (2,3) and

the nature of the invention is prevention of vasospasms which would require they do not present in the patient who is being treated at all (4) and the state of the prior art is such that prevention, especially when related to complicated diseases such as cardiovascular diseases is not well known or well established as evidenced by Graham et al. (US 2008/0267975 A1 on page 1, [0006]) (5) and while the skill of those in the art is high (6) the unpredictability of such a treatment is also high (7). The breadth of the claims is fine (8).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 5-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Batchelor et al. (British Journal of Pharmacology, 2001, vol. 132, pages 302-308, cited on applicant's IDS).

In claim 5, applicant claims a method for prevention or treatment for vasospasms accompanying a bypass operation, comprising: administering an effective amount of fasudil or hydroxyfasudil to a person in need of fasudil or hydroxyfasudil. The claimed method never requires administering to a patient that has vasospasms or a bypass operation, the only requirement is that the person be "in need" of the fasudil. Batchelor et al. teaches using fasudil (also referred to as HA1077) to treat patients undergoing coronary artery bypass surgery (page 303, column 1, paragraph 5) and they teach that HA1077 reversed submaximal contraction (page 304, column 1, paragraph 3) and they further teach that Rho-kinase inhibitors (of which HA1077 is as noted on page 304) are effective at preventing vasospasms in humans (page 307, column 2, paragraph 3). Thus the method of Batchelor et al. clearly anticipates claim 5, both inherently and also because they teach its effectiveness for treating vasospasms connected to coronary arty bypass surgery.

In claim 6, applicant specifies that the bypass operation is coronary artery bypass grafting and in claim 7 applicant specifies that the vasospasm treated is one that does not respond to a calcium antagonist. In claim 8, applicant specifies that the vasospasm occurs in a different region from an anastomosis region. Since these claims depend from claim 5, which does not actually limit the patient to those undergoing a bypass operation or having vasospasms, the method of Batchelor et al. inherently anticipates claims 6-8 as the method of administering the same drug to the same patient as claimed in the instant invention would have the same effect. Thus claims 6-8 are also anticipated by Batchelor et al.

Claims 5-8 are rejected under 35 U.S.C. 102(e) as being anticipated by Inokuchi et al. (J. Cardiovasc. Pharmacol., 2004, Vol. 44, No. 3, pages 275-277).

It is noted that Inokuchi et al. is published in September of 2004, which is between the current effective filing date of January 27, 2005 and applicant's claim to foreign priority of January 29, 2004. Since there is no English translation of that priority document priority has not been perfected yet and Inokuchi et al. qualifies as prior art. There is one common author as the inventor Hiroaki Shimokawa is listed on both documents, however since Inokuchi et al. cites 8 other authors it qualifies as "by another".

In claim 5, applicant claims a method for prevention or treatment for vasospasms accompanying a bypass operation, comprising administering fasudil or hydroxyfasudil. In claim 6, applicant specifies that the bypass operation is coronary artery bypass grafting and in claim 7 applicant specifies that the vasospasm treated is one that does not respond to a calcium antagonist. In claim 8, applicant specifies that the vasospasm occurs in a different region from an anastomosis region. Inokuchi et al. teaches that fasudil is effective for suppressing coronary artery spasms (abstract) and specifically teaches treatment of vasospasms which occur after coronary artery bypass grafting that do not respond to isosorbide dinitrated (ISDN) and that the vasospasm occurs in the artery that was not treated (pages 275-276, case 1). Thus Inokuchi et al. clearly teaches the same method as applicant and anticipates claims 5-8.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 5-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Batchelor et al. (British Journal of Pharmacology, 2001, vol. 132, pages 302-308, cited on applicant's IDS) in view of Satoh et al. (Jpn. J. Pharmacol., 2001, Vol. 87, pages 34-40).

In claim 5, applicant claims a method for prevention or treatment for vasospasms accompanying a bypass operation, comprising administering fasudil or hydroxyfasudil. In claim 6, applicant specifies that the bypass operation is coronary artery bypass grafting. Batchelor et al. teaches treatment of coronary artery bypass surgery with HA 1077, also known as fasudil (on page 304, column 1, third paragraph). They further teach that vasospasms are a problem in coronary artery surgery (abstract). Satoh et al. teaches that both fasudil and hydroxyfasudil, which is a metabolite of fasudil, protect the heart against vasopressin and inhibit Rho-kinase (abstract). They further teach that fasudil may have beneficial effects in treating coronary vasospasm (page 34, column 2, paragraph 2). It would have been obvious to one of ordinary skill in the art at the time of the invention that fasudil, and the active metabolite hydroxyfasudil, would be useful for

treatment of vasospasm in patients undergoing coronary artery bypass grafting. Batchelor et al. teaches the use in treatment of the surgery and Satoh et al. also teaches that that drug inhibits Rho-kinase, protects against vasopressin, and has beneficial effects against coronary vasospasms. This would suggest to one of ordinary skill in the art at the time of the invention that fasudil could be used to treat vasospasms, especially those related to coronary artery bypass grafting. Thus claims 5 and 6 are unpatentable over Batchelor et al. in view of Satoh et al.

In claim 7 applicant specifies that the vasospasm treated is one that does not respond to a calcium antagonist. In claim 8, applicant specifies that the vasospasm occurs in a different region from an anastomosis region. In both claims 7 and 8, applicant clams specific characteristics of the vasospasm that is treated and while Batchelor et al. and Satoh et al. doe not specifically mention whether the vasospasm had responded to calcium antagonists or occur in a region other than the anastomosis region, given the teachings of Batchelor et al. and Satoh et al. it would have been obvious to one of ordinary skill in the art at the time of the invention to use fasudil for any vasospasm that occurred in the coronary arteries regardless of cause and thus claims 7 and 8 are also unpatentable over Batchelor et al. in view of Satoh et al.

Conclusion

No claims are allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Meghan Finn whose telephone number is (571) 270-3281. The examiner can normally be reached on 9:30am-7pm Mon-Thu, 9:30am-6pm Friday (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Meghan Finn

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614